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Visual short-term memory binding in Alzheimer's disease and depression

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Abstract The differential diagnosis between Alzheimer's disease (AD) and major depression (MD) in the elderly can be problematic because the cognitive profile of the two conditions overlaps. Associative learning tasks seem to separate AD from MD. However, they are sensitive to the effects of normal ageing. Short-term memory-binding tasks have proved insensitive to the effects of normal ageing and highly sensitive to AD. However, they have not been used to differentiate AD from MD. The present study was aimed at investigating visual short-term memory binding in AD and MD. Fourteen AD patients, 14 patients with MD, and 14 healthy older adults were asked to perform a visual short-term memory binding task that investigated the retention of shapes, colors, or combinations of shapes and colors. Participants were to recognize changes occurring between two consecutive displays either in a single dimension (i.e., shape or color only) or in two dimensions (i.e., shape-color binding). Short-term memory performance for shape or color only was equivalent across groups. The only significant effect found was in short-term memory for shape-color binding and this was due to AD patients performing poorly in this condition only. The results extend previous findings in AD to visual short-term memory and suggest that the specific impairment in binding information in memory differentiates between the performance of AD and patients with MD.

Keywords Alzheimer's disease, major depression, short-term memory, memory binding, working memory, early detection

Introduction

The differential diagnosis between early Alzheimer's disease (AD) and major depression (MD) in the elderly can be problematic [4, 16, 22, 71, 79]. MD can precede AD and occur in the early stages of the disease [9, 30, 34, 35, 39, 42]. Moreover, the neuropsychological tasks currently used to assess AD are performed poorly by patients with MD (e.g., memory, attention, and executive functions) [2, 13, 37, 75]. Therefore, more specific methods are required to differentiate between the two conditions. Poor performance on episodic memory tasks have long been thought to characterize AD [17, 70]. However, memory dysfunction appears to occur in both AD and MD [2, 3, 9, 30, 34, 35, 39, 42, 46, 75, 88], suggesting that tests of episodic memory might be sensitive but not specific to AD. As a result, several memory tests and batteries of tests have been proposed to disentangle the two conditions [16, 17, 28, 41, 51, 88]. However, none of these measures appear to combine sensitivity with specificity for AD when subjected to rigorous testing [24, 28, 45].

Paired associate learning tasks have been reported to be particularly sensitive to AD and much less so to MD [5, 16, 25, 79]. Swainson et al. [79] reported that performance on the Paired Associates Learning Task of the Cambridge Neuropsychological Test Automated Battery (PAL-CANTAB), a cued recall task that

assesses the learning of object-location associations, resulted in 7% of overlap between AD patients and healthy controls/depressed patients (the scores of the last two groups were collapsed for such comparisons). In contrast, the Warrington SRMT with words and faces, showed overlaps of 99 and 78%, respectively. Dierckx et al. [16] used the visual association test (VAT) [47] and the memory impairment screen (MIS) [10] to produce a combined VAT-MIS score and compared performance of AD, MD, and mild cognitive impairment (MCI) patients. The combined score yielded a sensitivity of 83% (58%) and a specificity of 85% (85%) for differentiating AD (MCI) from MD.

Are such cued recall tasks that assess associative learning the solution for the early detection of AD and its differential diagnosis from depression? To answer this question, we would like to address some caveats regarding the studies discussed above. Firstly, the PAL-CANTAB task used by Swainson et al. [79] does not separate the contribution of item memory and associative memory from the deficits in recalling complex events. There is evidence suggesting that AD affects visuo-spatial memory [36, 57, 74] and particularly memory for item locations [7, 43, 77]. Hence, the PAL-CANTAB task does not assess the extent to which these object-location associative memory deficits can be accounted for by deficits in recalling locations only. Secondly, there are two issues concerning the methodological approach used by Swainson et al. [79] which may prevent a clear-cut assessment of their hypotheses. In their analysis the authors merged depressed and control participants in one single group and compared this to AD patients. Hence it is unclear how many depressed patients were actually better than the AD patients. Moreover, this may have resulted in dramatically low overlapping values because the size of the to-be-compared group was increased by including participants that were completely healthy. The results of the neuropsychological assessment shown by Swainson et al. [79] also revealed dramatic differences between depressed patients and controls in tasks such as logical memory (30 min recall), doors recognition, pattern recognition, category fluency, and others. Therefore, the actual contribution of the PAL-CANTAB task to the differential diagnosis of AD and depression cannot be clearly maintained from this study. Thirdly, in the paper by Dierckx et al. [16] no information on the neuropsychological assessment of depressed patients was presented. Hence, it is difficult to determine the actual contribution of the combined VAT-MIS score relative to other more traditional tasks.

Furthermore, the results reported by Dierckx et al. [16] are complicated by the fact that the depressed patients included in the study (but not the AD patients) were under treatment with antidepressants, which are known to improve performance on hippocampal-related tasks such as cued recall [38]. Lastly, the tasks reported by these authors [16, 79] assess associative learning, a function that has proved to be affected in normal ageing [12, 15, 58–63].

Recently it has been demonstrated that a different associative memory task, namely, short-term memory (STM) binding has been found to be substantially impaired in AD. Verbal STM-binding deficits were reported in patients with late-onset sporadic AD [67]. Contrary to associative learning, binding information in visual STM has been found to be preserved in normal ageing [8, 68]. This represents a step forward in the assessment of age-related disorders, as other forms of STM and LTM binding have been found to be impaired in older adults [14, 59, 62, 63]. In particular, the specific requirement of binding items to their spatial locations seems to make memory-binding tasks more sensitive to the effect of normal ageing [14, 55, 56].

Research on visual memory binding suggests that the efficiency of the mechanisms responsible for representing these complex events in memory may be sensitive to age [63], brain pathology [66, 67], and to methodological manipulations in experiments involving healthy young participants (e.g., type and amount of information, retention interval, availability of long-term representations, etc.) [1, 48, 86]. For example, holding in visual STM a “blue apple” and a “pink book” is a task efficiently performed by older people [67]. However, holding in visual STM an “apple on a TV” and a “book on a refrigerator” may be

an extremely difficult task for older adults (see [56]). Retaining in visual STM “shapes only” or “colored shapes” results in no behavioral difference in healthy young or older participants [8, 29]. However, retaining in visual STM “unicolored objects” or “bicolored objects” results in a dramatic drop in performance in the latter task regardless of age [68]. One common mechanism underlying successful performance in these tasks is the requirement of linking (i.e., binding) different features across different dimensions (i.e., color, shape, or location) or visual streams (i.e., ventral or dorsal). It might be possible that the differences observed across studies arise from the different demands of these tasks to develop effective connectivity across or within these feature dimensions [31, 33, 64].

Nevertheless, we have consistently found that the STM-binding functions investigated here are not differentially impaired in normal ageing. This allows us to reliably use these tasks to assess STM-binding in age-related disorders such as AD and MD. In fact, visual STM binding has not been previously used to assess patients with late-onset sporadic AD and neither has visual STM binding been used to discriminate between AD and MD in the elderly. This study was aimed at investigating visual STM binding in AD and MD.

Methods

Participants

Three groups of participants were recruited for the study. One group consisted of 14 patients with AD diagnosed according to the criteria established by the DSM-IV-TR and the NINCDS-ADRDA [53]. A second group consisted of 14 patients diagnosed with chronic depression (mean global depression scale score = 16.4, SD = 5.9; mean depression duration (from time of initial contact with services about depression to testing) = 11.3 years, SD = 9.11) according to the criteria established by the DSM-IV-TR. The third group involved 14 healthy older adults. Patients were referred by old age consultants. Healthy older adults were recruited through the panel of volunteers of the Psychology Department of the University of Edinburgh. All participants gave their informed consent to take part in the study. The study was approved by the relevant ethics committees.

The inclusion criteria set for the study were: (1) Normal color vision as assessed by the color blindness test [18]. (2) No other neurological or psychiatric disorders. (3) Score above 14 for the AD patients in the mini mental state examination (MMSE) [23]. (4) When possible, a brain CT or MRI scan ruling out cerebrovascular diseases. (5) Depressed patients were not taking tricyclic antidepressants. (6) Normal perceptual binding functions as assessed by the task described below. An additional inclusion criterion for the AD patients was (7) no history of chronic depression and no antidepressant medication at the time of assessment.

Perception for shape-color binding was assessed with a task that simultaneously presented two arrays of four colored shapes each, one in the upper half of the screen and one in the lower half. On each of the 20 trials, participants searched for changes between the two arrays. The arrays and the changes were the same as those described below for the shape-color binding condition. Participants with visual search accuracy below 90% (18 out of 20 trials correct) were not assessed further. None of the patients or healthy older adults recruited for the study was excluded due to perceptual binding problems.

The three groups of participants were matched according to age, gender distribution, and the number of years spent in formal education. Additionally, healthy older adults and depressed patients were matched according to their MMSE scores. The demographic and psychometric characteristics of the three groups of participants are shown in Table 1.

Assessment

The assessment consisted of two parts, a Neuropsychological Battery and a visual STM Task. The Neuropsychological Battery comprised the Addenbrooke’s Cognitive Examination [54] which incorporates the Mini Mental State Examination, Recall and Recognition of Word Lists [85], Letter (FAS)

Fluency, Trail Making Test Parts A and B [72], The Complex Figure of Rey-Osterrieth Copy and Delayed Recall [65, 73].

The visual STM task presented visual arrays of two or three stimuli each on a 15-in. flat TFT screen controlled by a laptop personal computer. Stimuli for each array were randomly selected from one set of eight shapes and one set of eight colors (see Fig. 1a for the set of shapes used). At the beginning of each trial, a fixation screen was presented for 500 ms. This was followed by the study display presented for 2,000 ms. After a blank retention interval of 900 ms, the test display was presented. On 50% of trials, the study and test displays were identical. On the other 50%, there were changes between the study and test display. The task for the participant was to detect when a change had occurred and to respond orally 'same' or 'different' as appropriate. Items randomly changed locations between trials, and were shown in different random locations for study and test arrays. This rendered location an irrelevant feature to the task, so location could not be used as a memory cue. The experimenter entered participants' responses using the keyboard. There was then a gap of 1,000 ms until the next trial (see Fig. 1b).

The STM task consisted of three conditions. Two conditions assessed visual STM for single features and one assessed the binding of these features in visual STM. In the Shape only and Color only conditions, the study arrays consisted of black shapes or colors (Fig. 1b). In the test display for the different trials, two new shapes or new colors from the study array were replaced by new shapes or new colors. In the Shape-color binding condition, the arrays consisted of combinations of shapes and colors. In the test display for the different trials, two shapes swapped the colors in which they had been shown in the study display. Hence, memory for bindings of shape and color in the study display was required in order to detect this change. In none of the three conditions were features repeated within a given array. For each condition there were 15 practice trials followed by 32 test trials. Trials were fully randomized across participants and conditions were blocked and delivered in a counterbalanced order. All the participants performed the visual STM task described above. Figure 1b shows an example trial for each experimental condition.

Statistical analysis

The array sizes used in the task for all participants were two and three items. However, post-hoc analyses suggested that performance levels in memory for single features would be similar across groups and floor and ceiling effects would be avoided when comparing AD patients with two items and MD patients and controls with three items. This follows our standard procedures (e.g., [49, 50, 67]) for comparing the impact of experimental manipulations on patients and controls. Reducing group differences in conditions assessing memory for single features, which provided baseline performance for investigating binding, would determine whether any differences between groups on STM-binding performance could be attributed to the binding requirement and not to baseline differences in memory for single features. In other words, this would rule out poor performance in the binding condition due to increased memory load. Therefore, AD patient's performance with only two items and controls' and depressed patients' performance with only three items were analyzed further (performance of the three groups with the two set sizes can be found in Supplementary Material).

Initial ANOVA and Chi-square analyses revealed that age and gender distributions did not differ across groups. Further, ANCOVA with age and gender as covariates showed that these factors did not modify the main outcomes nor did they interact with other independent variables (i.e., Group or Condition). Therefore, these factors were not further considered in statistical analyses. Subsequent two-way mixed ANOVA was performed. The between-subjects factor was Group (healthy older adults vs. depressed patients vs. AD patients) and the within-subjects factor was Condition (shape only vs. color only vs. shape-color binding). To assess significant interactions, post-hoc comparisons were carried out across groups for each condition separately ($3 \times 3 = 9$ contrasts) and across conditions for each group separately ($3 \times 3 = 9$ contrasts). With a total of 18 pairwise comparisons, the Bonferroni corrected alpha level was set at 0.003. Two measures of the signal detection theory were calculated for the analysis [76].

Sensitivity for the change detection (A') and response bias (Beta) were entered as the dependent variables.

Finally, ROC analysis was carried out to investigate the accuracy with which the STM task presented here can detect AD and differentiate this condition from MD. In doing so, we calculated the sensitivity, specificity, and positive and negative predictive values for each score of the STM task.

Results

Neuropsychological assessment

The analysis of the MMSE showed that patients with depression and controls had a similar cognitive level, while the cognitive level of AD patients was significantly lower than that of the depressed and control participants. Independent sample t-tests showed that depressed patients performed significantly better than AD patients in all the neuropsychological tasks used (Table 2). When the individual scores were compared to published normative data (cut-off values), depressed patients' memory performance (i.e., Word List and the delayed recall of the Rey Figure) and attention (TMT part B) was found to be below cut-off in around 50% of the patients while almost 100% of the AD patients performed below cut-off. This suggests that although, at a group level, depressed patients were at a better cognitive level than AD patients, in memory and attention around half of them performed below the normality threshold. This would have made it difficult to distinguish which patient belonged to which group on the basis of these measures alone.

Visual STM task

A' analysis

Mean sensitivity data are shown in Fig. 2a. Significant main effects were found for Group [$F(2,39) = 20.1$, $p < 0.001$], for condition [$F(1.26,49.36) = 37.74$, $p < 0.001$], and for the interaction between these factors [$F(2.53,49.36) = 12.2$, $p < 0.001$].

Bonferroni-corrected post-hoc tests carried out on the main group effect showed that controls and depressed patients did not differ whereas both performed significantly better than AD patients ($p < 0.001$ in both cases). Bonferroni-corrected pairwise comparisons carried out on the main effect of conditions showed that performance in the condition assessing STM for shape only and color only did not differ and both were better than performance in the condition assessing STM for shape-color binding ($p < 0.001$ in both cases).

In order to assess the interaction, post-hoc tests were carried out across groups for each condition separately. This showed that depressed patients and controls did not differ in any of the experimental conditions and both groups performed significantly better than AD patients only in the condition assessing STM for shape-color binding ($p < 0.001$ in both cases). Comparisons carried out across conditions for each group separately showed that the performance of controls and depressed patients did not differ in any contrast. The performance of AD patients in the conditions assessing STM for shape only and color only did not differ and both were significantly better than performance in the condition assessing STM for shape-color binding ($p = 0.001$ in both cases). Therefore, these results suggest that the significant group by condition interaction was solely driven by the poor performance of AD patients in the condition assessing STM for shape-color binding.

Beta analysis

Figure 2b shows mean response bias (Beta) data for the three groups in the three conditions. Significant main effects were found for group [$F(2,39) = 3.87$, $p < 0.05$], for condition [$F(2,78) = 12.45$, $p < 0.05$], but not for the interaction [$F(4,78) = 2.36$, n.s.].

Bonferroni-corrected post-hoc tests carried out on the group effect showed no difference in response bias across the three groups. Bonferroni-corrected pairwise comparisons carried out on the main effect of conditions showed that STM performance in the condition assessing shape-color binding

resulted in a greater response bias than did the condition assessing shape only ($p = 0.003$) and color only ($p < 0.001$). Response bias in the last two conditions did not differ. Therefore, these results suggest that a preference for a particular response (i.e., same or different) did not account for the poor sensitivity observed in AD patients.

Classification analysis

ROC analysis confirmed that only the task assessing the binding of information in STM combines sensitivity and specificity for AD (Fig. 3). ROC analysis revealed that with a cut-off value for A' of 0.85, a sensitivity of 86% and a specificity of 100% for AD were achieved. This cut-off value yielded positive and negative predictive values of 100 and 88%, respectively. No other task used in the assessment achieved this classification power. Using the same cut-off value, the STM-binding task proved insensitive to MD (sensitivity = 14%, specificity = 93%, positive predictive values = 67%, negative predictive values = 54%).

Discussion

The results of the present study revealed that visual STM binding is impaired in late-onset sporadic AD. This extends previous findings of verbal STM-binding deficit in AD [67]. Taken together, the findings suggest that STM-binding deficits in AD are not restricted to a particular memory domain (i.e., visual or verbal) or to a specific retrieval process (i.e., recall or recognition), but are a fundamental impairment of AD. Moreover, we have found that visual STM binding discriminates between AD and MD in the elderly with high sensitivity.

It is worth noting that the results presented here were obtained using a task that firstly separates the contribution of item memory and memory binding to the representation of complex events in STM [67], and secondly has proved to be insensitive to the effects of age [8, 68]. Further evidence for the latter is given in the present study in which the performance of older controls was equivalent across the three experimental conditions. With this methodology we have demonstrated that even when AD patients' performance in tasks assessing memory for individual features is equivalent to that of controls and MD patients, they present with paramount difficulties in retaining in STM the binding between these features. This suggests that STM-binding deficits are specific to AD and that these deficits are much greater than other memory impairments for individual items.

Although many of the depressed patients were impaired on a range of traditional memory tasks (e.g., Word List recall), they did not differ from our control group in any of the conditions used in the STM-binding task. The reason for this normal performance may be that the STM-binding task was based on a change detection paradigm that assesses recognition. There is agreement that recognition is generally a less demanding task than recall [40, 51, 52] and that within recognition tasks, change detection tasks are even less demanding [14]. The reason is that in change detection tasks the role of familiarity is crucial as both test and probe phases present the same items in 50% of the trials [14, 69].

This is relevant to the discussion of the possible effects of depression on memory performance. There is neuroimaging evidence suggesting that, as compared to controls, depressed patients show functional, but not behavioral, changes in memory processing of face-profession associations [84, 87]. The authors suggested that the functional changes may reflect compensatory activity responsible for maintaining the level of performance of depressed patients at a level equivalent to that of the control participants ([84] see also [11] for a review on the neuroanatomical implications of chronic depression). These compensatory changes, however, seem to be less efficient as the task demands increase. There is agreement that to achieve high sensitivity and specificity in the differential diagnosis between AD and MD, the tasks used should not have high cognitive demands as the performance of depressed patients may drop dramatically when the difficulty of the tasks increases [6, 16, 19, 20, 37]. For example, tasks assessing free recall (e.g., prose recall, word list recall, etc.) are poorly performed by depressed patients [19]. However, tasks assessing cued recall are performed by depressed patients with less difficulty [16, 79].

These findings have been explained by postulating that cues are used as memory aids, hence less cognitive effort is required (e.g., in the current change detection task features or bindings are shown at encoding and probe phases). However, in free recall tasks, the reliance on contextual information is higher and the tasks are more cognitively demanding [16]. Free recall seems to be more dependent on the hippocampus, a region that has been found to be impaired in middle-aged depressed patients even after their first episode of depression [27].

In fact, the compensatory changes found in the fMRI studies mentioned above were observed with tasks presenting face-profession pairs at encoding and faces as cues at test [84, 87]. Frodl et al. [26] observed increased connectivity in the prefrontal regions in depressed patients during a face-matching task. This suggests that brain changes occurring in the form of new compensatory connections may underlie normal performance of depressed patients on relatively low-demanding tasks. However, these types of changes are less likely to occur in AD as the main pathological outcome of the disease is loss of brain connectivity [32, 83, 89]. This can help to explain why AD patients are less able to bind in memory the different elements of complex events as accurate binding requires efficient connectivity at a neuroanatomical level [82].

The task presented here has demonstrated that it is the binding of different pieces of information together rather than memory for individual features that is more severely affected by AD and which can differentiate AD from MD patients. As compared to LTM and attention functions, STM binding proved to be more successful at differentiating between AD and MD. In the condition assessing shape-color binding, only five out of 14 depressed patients fell below cut-off whereas in the word lists recall task, 14 out of 14 depressed patients fell below cut-off (using 95% CI). This is in contrast with the results of the AD group in which 13 out of 14 and 14 out of 14 patients fell below cut-off in the shape-color binding condition and in the word lists recall task, respectively. These results were further supported by a classification analysis (using ROC methodology) which confirmed that the STM-binding task combines sensitivity and specificity for AD and is insensitive to MD. Notably, these results with the STM task were obtained when no significant differences were found in performance on conditions assessing memory for single features (i.e., shape or color only) across the three groups. It is worth noting that the paramount binding deficit observed in AD patients was not restricted to the set size chosen for the analysis presented here (i.e., two items). The reason for this selection was explained above. When AD patients were assessed with visual arrays of three items, STM for bindings was still much poorer than STM for single features (see Supplementary Material). This suggests that the specificity of the STM-binding deficit observed in AD does not reflect a general memory limitation resulting from increased memory load.

One other study in which a different working memory component was used to address the issue of the differential diagnosis between AD and depression was that by Kaschel et al. [44]. In this study, the authors asked AD and depressed patients to perform two concurrent tasks one of which was delivered at the individual span (i.e., digit span). The function of the executive component of working memory was measured by computing the cost of performing two concurrent tasks as compared to performing each task separately. The authors reported that AD patients presented with paramount difficulties performing two concurrent tasks whereas depressed patients' performance was similar to that of controls. These previous findings and the current findings lead to the suggestion that, including working memory tasks in the assessment, such as the STM binding task reported here, would enable the separation of depressed patients from AD patients more accurately than when other more traditional tests of memory and attention are used. The results reported in the current study were obtained with a relatively small sample of AD and MD patients. Notwithstanding the specificity of the STM-binding deficit in AD was corroborated through ANOVA and ROC analysis. Future studies should investigate whether the results presented here also characterize a larger sample of patients.

In conclusion, STM-binding deficits may be conceived as a fundamental marker of AD. These impairments seem to extend across memory systems (i.e., STM and LTM), memory domains (i.e., verbal and visual), retrieval mechanisms (i.e., recall and recognition) and clinical forms of AD (i.e., late-onset

sporadic AD and early onset familial AD). The present study provides novel insights in suggesting that AD affects the mechanisms responsible for binding information in visual STM in a significantly larger proportion of patients than depression. As STM-binding tasks have proved to achieve high sensitivity and specificity in detecting AD, they may be proposed as useful and complementary tools for the assessment of AD and MD in clinical settings.

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Tables and Figures

Table 1. Demographic and psychometric characteristics of participants entering the study

	Healthy controls (n = 14)		Depressed patients (n = 14)		AD patients (n = 14)			P-value
	M (SD)	Range	M (SD)	Range	M (SD)	Range		
Age	70.71 (4.30)	65–79	72.71 (7.54)	60–82	76.29 (5.78)	65–84	F (2,39) 3.07	0.06
Gender (M/F)	07-Jul		04-Oct		07-Jul		χ^2 (df = 2) 1.75	0.42
Years of education	15.57 (3.32)	10–23	13.43 (3.01)	9–18	12.71 (3.77)	8–20	F (2,39) 2.71	0.08
VIQ	107.93 (14.48)	60–118	113.00 (7.24)	100– 126	106.36 (6.77)	94–119	F (2,39) 1.64	0.21

One-way ANOVA. None of the Bonferroni-corrected post-hoc tests resulted in significant differences; VIQ verbal IQ as measured by Wechsler Test of Adult Reading

Fig. 1

a Shapes used to construct stimuli arrays. **b** Experimental conditions and trial designs

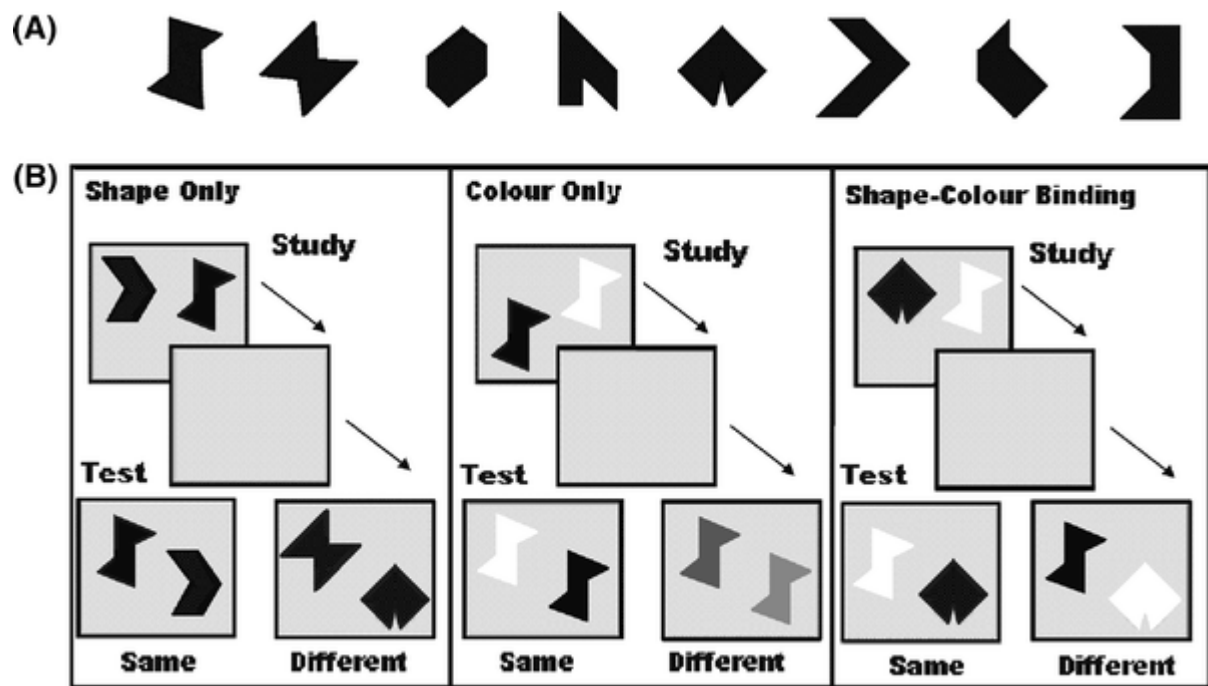


Table 2. Results of the neuropsychological assessment and the STM-binding task

	Cut-off	Healthy controls (n = 14)		Depressed patients (n = 14)		No. below cut-off	AD patients (n = 14)		No. below cut-off
		M (SD)	Range	M (SD)	Range		M (SD)	Range	
MMSE ^a	24	28.83 (1.47)	26–30	28.21 (1.37)	25–30	0	23.36 (2.73)	17–27	10
ACE ^b	84 ^d			90.93 (5.38)	82–99	2	64.64 (11.71)	40–79	14
Word list I (recall) ^b	29 ^c			6.93 (3.41)	0–11	14	0.79 (1.81)	0–5	14
Word list II (recognition) ^b	23 ^c			22.00 (1.92)	19–24	7	14.36 (3.03)	7–18	14
Letter fluency (FAS) ^b	22 ^d			42.21 (10.56)	24–59	0	24.86 (12.11)	8–50	8
Verbal fluency (animals) ^b	12.1 ^d			17.79 (4.10)	9–24	1	9.07 (4.91)	2–18	10
TMT part A ^b	57.6 ^d			47.86 (16.87)	28–83	4	138.42 (139.36)	28–502	11
TMT part B ^b	145 ^d			129.50 (48.30)	52–213	6	305.00 (164.60)	87–732	13
Rey figure (copy) ^b	31 ^c			34.52 (1.83)	30–36	1	26.89 (11.74)	4–36	5
Rey figure (delayed recall) ^b	13 ^c			11.43 (8.94)	0–27	9	3.18 (4.79)	0–13	13
Shape only (A')	0.95 ^e					3			6
Color only (A')	0.98 ^e					6			8
Shape-color binding (A')	0.91 ^e					5			13

^aAD patients different from controls and depressed patients at $p < 0.05$ (one-way ANOVA—post-hoc tests)

^bDepressed and AD patients different at $p < 0.05$ (Independent sample t tests)

^c5th percentile taken from standardized age-matched normative data

^dMean and SD taken from standardized age-matched normative data

^eLower bound of the CI at 95% calculated from controls; MMSE Minimental State Examination; M (SD) mean and standard deviation; norms from: ACE [54]; word list [85]; letter fluency (FAS) [78]; verbal fluency (animals) [81]; TMT [80]; Rey Figure [21]

Fig. 2.

a Mean sensitivity data (A') and **(b)** mean response bias in the group by condition analysis (Error bars represent the standard errors of the mean)

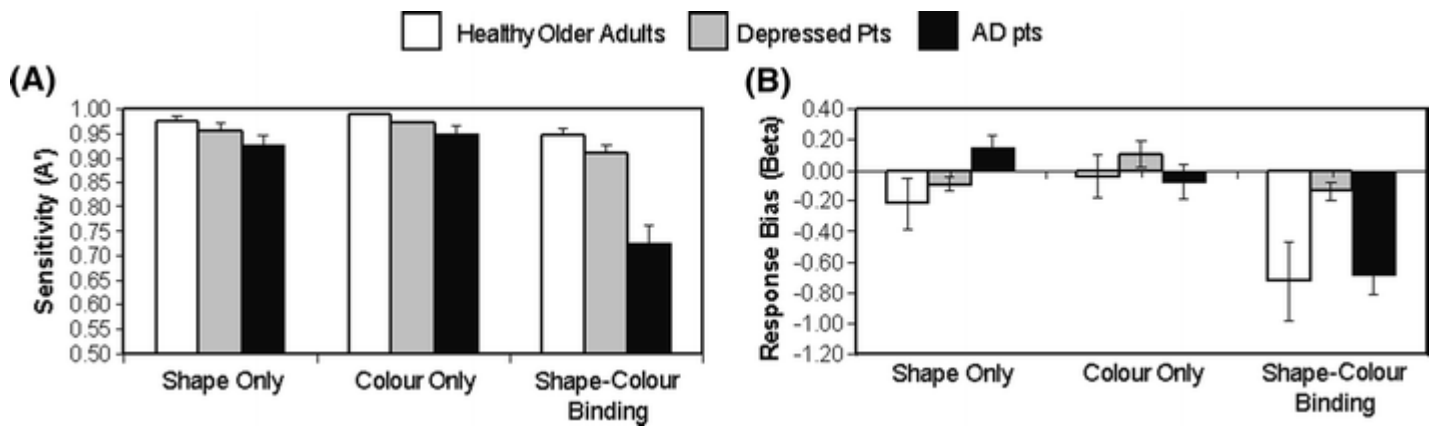


Fig. 3. ROC analysis with the three conditions of the visual STM task in **(a)** AD and **(b)** MD patients

